EXECUTIVE SUMMARY

# VISION RESEARCH

## A NATIONAL PLAN

1983-1987



U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
Public Health Service
National Institutes of Health


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# FOREWORD

*THE MISSION OF* the National Eye Institute is straightforward: find new ways to prevent, diagnose, and treat diseases of the visual system, thus preventing, reducing, and possibly even eliminating blindness. Although this mandate is explicit, recent developments in scientific concepts and technology have been so prolific that no one individual, no matter how well informed, can understand and appreciate them all, let alone know which research should be emphasized so that society will benefit maximally. Optimal distribution of the research dollar, whether Federal or philanthropic, is extremely difficult, but especially in times of fiscal stringency, it is a goal we must strive toward.

Thus, we, the members of the National Advisory Eye Council, with the aid of numerous experts from the scientific community, have in *Vision Research—A National Plan: 1983-1987* documented the extent of the problem of visual disorders and blindness and assessed virtually all current research aimed at its solution. Based on this appraisal we have outlined what we believe to be today's most urgent research needs and examined existing and potential opportunities for meeting them. Furthermore, because we believe we should not merely list such opportunities, but evaluate their likelihood of succeeding, we have set research priorities and estimated their cost.

We will implement these priorities by always supporting the best basic and clinical research proposals we receive and, when necessary, by taking special measures to help ensure that our goals are met. To accomplish this we seek the support of the vision research community, other scientists, and all those who share our interest in eradicating blindness and visual disability.

THOMAS D. DUANE, M.D., Ph.D.
Chairman
Program Planning Subcommittee
National Advisory Eye Council

# PREFACE

*THIS IS AN* Executive Summary of *Vision Research—A National Plan: 1983-1987,* a multivolume report prepared by the National Advisory Eye Council, the principal advisory body to the National Eye Institute (NEI). The complete plan presents a comprehensive and detailed assessment of the current NEI program along with specific recommendations for its development over the next five years. These include program priorities and projections of resource requirements for each major area of vision research that the NEI supports. Although the plan's major sections are briefly highlighted here, readers desiring additional information and detail should consult the following volumes:

*Volume One—The 1983 Report of the National Advisory Eye Council* (Background, Summary Panel Reports and Resource Requirements, Implementation Strategy, Cross-Cutting Research Areas and Issues, Planning Participants, Planning Strategy and Process).

*Volume Two—Reports of the Program Panels*

**Part One**—*Report of the Retinal and Choroidal Diseases Panel*

**Part Two**—*Report of the Corneal Diseases Panel*

**Part Three**—*Report of the Cataract Panel*

**Part Four**—*Report of the Glaucoma Panel*

**Part Five**—*Report of the Strabismus, Amblyopia, and Visual Processing Panel*

**Part Six**—*Report of the Panel on Visual Impairment and Its Rehabilitation.*

*Volume Three—Support for Vision Research* (Data on vision research projects supported by the NEI in FY 1981 and by other government and private organizations in FY 1980).

# EXECUTIVE SUMMARY

## INTRODUCTION

*EYE DISEASES AND* blindness cause suffering, disability, and loss of productivity for millions of people throughout the world. In the United States alone, over 10 million people suffer from visual impairment that cannot be corrected by eyeglasses or contact lenses. Of these people, 1.5 million are so severely impaired they cannot read ordinary newsprint. This includes approximately half a million who are legally blind.[1] The leading causes of blindness and visual disability in the United States are aging-related maculopathy,[2] cataract, glaucoma, diabetic retinopathy, and optic nerve atrophy.

Added to the physical and emotional pain and hardship these disorders cause is their staggering economic burden. Recent estimates indicate that eye disorders and blindness cost our nation more than $14 billion annually. Convinced that visual disorders constituted a major public health problem that could only be solved by placing greater emphasis on research, the United States Congress on August 16, 1968, authorized the establishment of a National Eye Institute as part of the Federal Government's National Institutes of Health.

[1]Legal blindness is defined as visual acuity of 20/200 or poorer in the better eye, even when wearing eyeglasses or contact lenses, or a field of vision no greater than 20 degrees in its widest diameter.

[2]The term used in this national plan to replace the more common but misleading designation "senile macular degeneration."

## NEI MISSION AND GROWTH

The mission of the new Institute, as the Congress specified in Public Law 90-489, its authorizing legislation, was to "conduct and support...research for new treatment and cures and training relating to blinding eye diseases and visual disorders, including research and training in the special health problems and requirements of the blind and in the basic and clinical sciences relating to the mechanisms of the visual function and preservation of sight."

The NEI's budget has grown from an initial appropriation in FY 1970 of $24 million, which included support for approximately 350 individual research project grants, to a budget of $118 million in FY 1981 which included support for nearly 900 such investigator-initiated awards. Today, the NEI funds approximately 80 percent of all vision research supported by the Federal Government and national private philanthropic organizations.

## ACCOMPLISHMENTS

Over the past 14 years, support for vision research provided by the NEI has led to numerous accomplishments and discoveries that have greatly advanced the assault on blindness and visual disability. Some recent examples include:

- Demonstration in two nationwide clinical trials that laser treatment can be highly effective in preventing or retarding severe visual loss from two leading causes of blindness: diabetic retinopathy and aging-related maculopathy.
- Improved early diagnosis of retinitis pigmentosa, an inherited disease that causes progressive loss of peripheral vision and night blindness, and development of a means for identifying the carriers of one genetic type of this disease.

- Development of vitrectomy, a surgical procedure for restoring vision lost from bleeding and scar tissue inside the eye due to diabetes and other disorders or trauma.
- Demonstration that the enzyme aldose reductase, previously shown to trigger the formation of cataracts in diabetic laboratory animals, may also be a cause of other diabetic complications. Development and clinical testing of drugs that inhibit the enzyme's action are underway to determine if they can prevent such complications in people with diabetes.
- Advances in the identification and isolation of agents that cause uveitis, a chronic, difficult to treat ocular inflammation, and the development of a promising new immunotherapy for this disorder.
- Identification of a specific enzyme defect in patients with gyrate atrophy, a rare retinal degenerative disease resembling retinitis pigmentosa, which may lead to a means of treatment.
- Identification of retinal neurotransmitters, chemical messengers that make communication possible between cells in the retina.
- Better understanding of the cellular properties of the retinal pigment epithelium and of the central role played by this single cell layer in the survival and function of the visual cells.
- Development and testing of new antiviral agents that have improved the treatment of ocular herpes simplex infection.
- Growth of corneal cells in laboratory culture and successful transplantation of these cells to animal eyes, offering hope for a new approach to corneal grafting that would greatly reduce the need for fresh donor tissue.
- Demonstration of the possible role of light and oxidation in causing human cataract, a finding that may lead to means of prevention.
- Successful use of the laser to treat acute angle-closure glaucoma and promising preliminary results from laser treatment of chronic open-angle glaucoma, the most common form of the disease.
- Growth in the laboratory of cells of the trabecular meshwork, the tissue through which aqueous fluid drains from the eye. Studies of these cultures are expected to demonstrate cellular processes that regulate fluid outflow and, when disturbed, play a role in the development of glaucoma.
- Improved understanding of the critical period in infancy during which inadequate visual stimulation due to cataract, strabismus, or some other impediment can cause lifelong visual impairment.
- Successful treatment of two eye movement disorders with drugs: baclofen to inhibit irregular eye movements (nystagmus) and botulinum toxin to restore ocular alignment in strabismus (cross-eye or walleye).
- Widespread application of modern clinical trial methodology to evaluate scientifically the safety and effectiveness of new methods of treating eye disorders and conditions.

For more information about these and other achievements in eye research made possible by NEI support, see *Volume One*, Chapter Three, and the Recent Accomplishments sections within each of the Reports of the Program Panels in *Volume Two*.

# VISION RESEARCH PROGRAM PLANNING

The legislation establishing the NEI authorizes the Secretary of Health and Human Services "to plan for research and training, especially against the main causes of blindness and loss of visual function." In response to this mandate and to the need to ensure stability, continuity, and accountability in Federal support for vision research, the NEI, in conjunction with its senior advisory body, the National Advisory Eye Council, began comprehensive program planning and evaluation in 1973, an effort that has continued to the present time.

Three national vision research plans have been prepared: the first for the fiscal years 1976-1979, the second for 1978-1982, and the present plan for 1983-1987. These published and widely distributed documents have outlined priorities for NEI support that are based upon detailed assessments of current needs and opportunities in vision research. The NEI has used these national plans to stimulate research in priority areas, to support the day-to-day and long-range management of the Institute, and to communicate program goals, accomplishments, and needs to a wide range of audiences.

# FEATURES OF THE 1983-1987 NATIONAL PLAN

Each time the Council has developed a new national plan, an attempt has been made to refine and improve the NEI program planning system. Thus, the strategies and methods used in vision research program planning have evolved over the years. The 1983-1987 plan is characterized by the following:

- Review and assessment of the entire National Eye Institute program, as well as vision research supported by other organizations, by more than 250 scientists representing all major areas of vision research.
- Revised NEI program structure to improve categorization of current research support and provide a framework for assessing future needs and opportunities in vision research.
- For each NEI program—Retinal and Choroidal Diseases; Corneal Diseases; Cataract; Glaucoma; Strabismus, Amblyopia, and Visual Processing—and for the special cross-program area of Visual Impairment and Its Rehabilitation, the plan:
  - Describes the diseases and disorders, including their public health impact, and the research disciplines that the program addresses.
  - Defines program goals and objectives.
  - Surveys current support by the NEI and other organizations.
  - Reviews recent program and research accomplishments.
  - Describes current research needs and opportunities.
  - Makes specific recommendations concerning program development.
- Discussion of how the vision research projects the NEI supports relate to the following cross-cutting health science areas and issues, several of which are the subject of considerable national interest for scientific, economic, social, or political reasons:
  - Prevention
  - Diabetes
  - Nutrition
  - Aging
  - Toxicology
  - Genetics
  - Immunology
  - Epidemiology
  - Neurobiology
  - Molecular Biology
  - Noninvasive Research and Diagnostic Techniques
  - Refractive Errors
  - Use of Animals in Vision Research
- For the first time, the Council's recommendations have been grouped according to two categories which together encompass all the research supported by the NEI:
  - *Program Base*—Research areas that should continue to be supported essentially at current levels of activity for the next five years.
  - *Program Development Priorities*—Research areas that warrant new or added support for the next five years.

# IMPLEMENTATION OF THE NATIONAL PLAN

The individual, investigator-initiated NIH research project grant continues to be the NEI's highest priority funding mechanism. For this reason, the successful implementation of this national plan will depend largely upon scientists submitting high quality grant applications for research in the areas recommended for emphasis by the Council and the planning panels. **Scientific merit, as assessed by evaluation of all applications in the traditional NIH peer review system, will continue to be the principal factor considered in determining which approved grant proposals the NEI will fund.** However, additional measures will be taken by the Council and NEI staff to help fulfill the plan's recommendations. These measures include:

- Designating some approved grant applications as having *High Program Relevance*, thereby placing them in a more favorable position for funding than would otherwise be the case.
- Encouraging the development of proposals for high quality *clinical research*, including clinical trials and other epidemiologic approaches.
- Encouraging *research training and career development* in the sciences related to vision, with particular emphasis on clinicians and other investigators who can help implement the priorities outlined in the plan.
- Sponsoring *scientific workshops* in selected priority areas to encourage exchange of scientific in-

formation and techniques among vision scientists and between vision scientists and investigators in other fields. Workshops will be held in areas in which interdisciplinary interaction is considered especially important to advancing the field, such as in ocular immunology.

- Supporting *core grants* to help maintain institutional environments which foster high quality collaborative research and multidisciplinary approaches among investigators who already have NEI individual research grant support.
- Funding *specialized clinical research centers* to support a group of clinical studies which have a common focus on the etiology, pathogenesis, diagnosis, or treatment of human visual disorders.
- Providing for the maintenance and distribution of *special research resources*, such as laboratory animal breeding colonies and human donor tissue, as well as establishing special arrangements, such as consortium grants, to pool scarce resources in cooperative endeavors related to the priorities of this plan.
- Selectively using *research contracts* or *cooperative agreements* to continue support of NEI-initiated multicenter clinical trials and for the procurement of special research resources.
- Using the *NEI intramural research program* to take advantage of the unique resources and environment of the NIH campus in carrying out the priorities of this plan and to serve as a national resource for the training and career development of basic and clinical vision researchers.
- Encouraging the *transfer of scientific knowledge and the dissemination of information* to practitioners and the general public to help in achieving the NEI's long-range goal to improve the visual health of the American people through research.
- Participating in *international activities and agreements* that provide a knowledge base for worldwide efforts to prevent blindness, broaden the scope of vision research generally, and bring about better utilization of research resources in participating countries.

Each of these measures is discussed in greater detail in *Volume One*, Chapter Four, "Implementation of Program Priorities."

# PANEL REPORTS

The 1983-1987 national plan is based upon six reports prepared by panels of leading scientists. These reports, covering the five NEI programs and the special topic of Visual Impairment and Its Rehabilitation, constitute the six sections of *Volume Two* of this plan.

The following description of the major components of the visual system serves as a reference for the subsequent brief descriptions of the NEI programs, each of which includes highlights of the Council's recommended Program Development Priorities. Additional information is included in the summary panel reports in Chapter Three of *Volume One*. The full panel reports in *Volume Two* contain a thorough discussion of each program, including all elements of the Program Base and Program Development Priorities and detailed estimates of resource requirements.

# THE VISUAL SYSTEM

Each portion of the eye and visual pathway depicted in Figures 1, 2, and 3 performs a specific function. The optical elements of the eye, the *cornea* and the *lens,* focus images onto the *retina*, a thin, light-sensitive surface lining the inside of the back of the eye. The *iris* regulates the amount of light falling on the retina by changing the size of the *pupil*. The two major functions of the *ciliary body* are to secrete *aqueous humor*, a clear fluid that nourishes the cornea and lens, and, by means of suspensory ligaments called *zonules*, to hold the lens in place and change its shape and thickness (a process known as accommodation) so that the eye can focus on objects at various distances. The *vitreous humor*, the clear gel that fills the center of the eye, helps maintain the eye's shape.

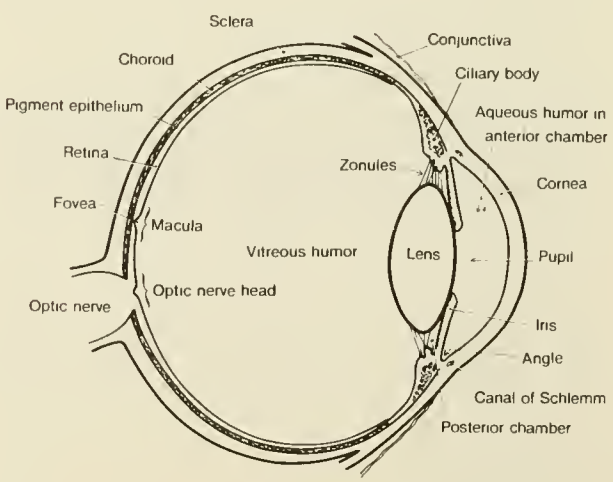


FIGURE 1. Cross section of the human eye.

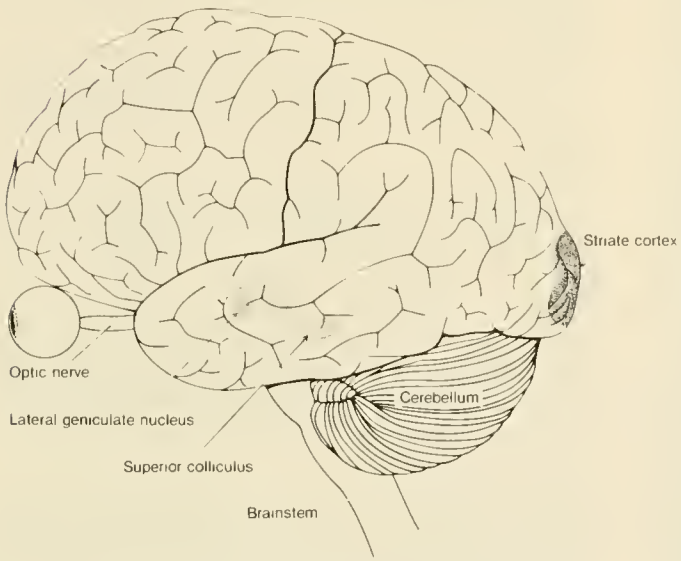


FIGURE 2. Lateral view of human brain, including interior visual pathway structures: lateral geniculate nucleus and superior colliculus.

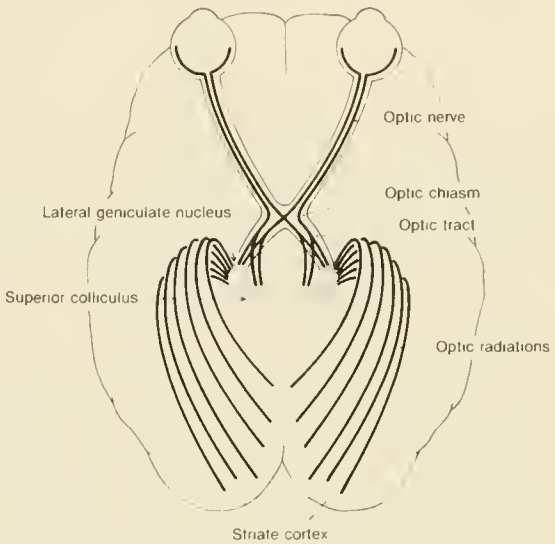


FIGURE 3. Visual pathway traced schematically in the human brain.

The transmission of visual information through the retina is a complex process. The retina's photoreceptor cells, called rods and cones, convert incoming light to electrical signals which are further processed and integrated by an exquisitely organized cellular system. The ganglion cells, the output cells of the retina, have been classified into functionally specialized types, each sensitive to different stimulus sizes, velocities, and locations in the visual field. Axons from the ganglion cells form the *optic nerve* and *optic tract*. These connect with the *lateral geniculate nucleus*, a group of cells in the thalamus of the brain. From there nerve impulses are sent to the *striate* area of the *visual cortex* at the back of the brain. The striate cortex is also a complex structure, divided into anatomically distinct layers and functionally separate columns of cells. Neurons in this area send axons forward to many other cells and back to many of the areas from which they receive input. Some retinal ganglion cell axons send branches into a region of the midbrain, the *superior colliculus*, which aids in orientation to objects or other visual stimuli through control of eye movements. Circuits of neurons in the *brainstem*, including their connections with the *cerebellum*, are also important parts of the eye movement system. Clearly, the visual system is highly organized and complex; a major portion of the brain is directly and exclusively involved in the visual process. This is consistent with the very great sensory importance of sight.

# RETINAL AND CHOROIDAL DISEASES

The normal functioning and survival of the retinal cells depend on a carefully controlled environment and a continuous supply of oxygen and nutrients supplied by two systems of blood vessels, one within the retina and the other in the highly vascular *choroid*, the tissue lying immediately underneath. Damage to the retina, interruption in its blood supply, or injury to the tissues with which it interacts, such as the *pigment epithelium* (a single cell layer between the retina and choroid that controls many nutritive exchanges between the blood and the retina) can lead to loss or severe impairment of vision. Unfortunately, the retina is susceptible to injury in numerous ways, including damage from systemic disorders such as diabetes and sickle cell anemia, infection and inflammation, circulatory failure, hereditary factors, aging, trauma, and toxic and environmental factors.

These disorders cause approximately 200,000 cases of legal blindness in the United States. Each year, 19,000 additional Americans become blind from retinal and choroidal diseases. One of these diseases, diabetic retinopathy, is the leading cause of new cases of blindness in adults under age 65, and another, aging-related maculopathy, is the leading cause of new cases of blindness in people age 65 and older.

Diabetes affects a number of eye tissues, but exerts its most harmful effects on the tiny blood vessels of the retina where it triggers a series of events that may lead to severe and irreversible visual loss. Timely laser treatment can halt the progress of advanced diabetic retinopathy and forestall blindness in a large percentage of cases. In some instances, when blood leaks into the vitreous humor, impaired vision can be improved through a surgical procedure known as vitrectomy. Although these advances have benefited thousands of people, the search continues for better methods to treat and for ways to prevent or cure diabetic retinopathy.

Disease of the *macula*, the small area of the retina that provides sharp central vision, occurs primarily with aging, affecting to some degree millions of Americans over age 50. When this disease becomes severe it is capable of depriving the elderly of the full enjoyment of their retirement years. In May 1982, a nationwide clinical trial sponsored by the NEI provided the first conclusive evidence that laser treatment, if carried out within days or weeks after onset of symptoms, can be highly effective in preventing severe visual loss from the neovascular type of aging-related maculopathy, which is characterized by the formation of abnormal new blood vessels between the retina and choroid near the macula. Most legal blindness from aging-related maculopathy is due to the neovascular form which affects approximately 116,000 people in the United States. Evidence from this study suggests that the vast majority of such cases of blindness could be prevented or delayed significantly by timely laser treatment if the disease is recognized early. Although these findings are impressive, much more research is needed to find better ways of treating and ultimately preventing aging-related maculopathy.

More research is also needed on retinal diseases that begin early in life, such as retinitis pigmentosa, a disorder that most often strikes young people during their critical learning years. This disease, for which there is no known cure or means of prevention, causes night blindness and a gradual restriction of the visual field. Those affected face a lifetime of visual impairment and disability.

Other common and disabling retinal and choroidal diseases are retinopathy of prematurity (retrolental fibroplasia) which causes blindness in premature infants, retinal detachment, uveitis, and retinal tumors. Intensive research over the last several years has led to dramatic improvements in the diagnosis and treatment of some retinal and choroidal diseases and in certain cases to means of restoring the visual loss they have caused. However, the fact that most of the serious diseases in this group are still poorly understood underscores the need for continued and intensified research.

The following are examples of the Council's recommended Program Development Priorities for the Retinal and Choroidal Diseases program:

- Exploiting technological advances in the fields of molecular biology, cell physiology, and tissue culture for basic research on retinal cells and tissues.
- Assessing new drug and immunological approaches to the treatment and prevention of uveitis and other inflammatory disorders.
- Expanding biochemical and metabolic studies of Bruch's membrane (which separates the retina from the choroid), the adjacent retinal pigment epithelium, and the photoreceptors in the central retina, to provide new insights into aging-related maculopathy, other retinal degenerations, and retinal detachment.
- Intensifying the search for biochemical and genetic defects in retinitis pigmentosa and other hereditary retinal degenerative diseases, utilizing new molecular biology techniques.
- Characterizing neurotransmitters, the chemical substances that relay messages from one retinal nerve cell to another, with the aim of developing drug therapies for retinal neural disorders.
- Developing and applying better noninvasive tests of retinal physiology and of visual function in normal and pathological conditions.
- Performing studies of retinal capillary cells in tissue culture to elucidate the mechanisms of neovascularization, the abnormal growth of new retinal blood vessels, and the hemorrhaging that occurs in diabetic retinopathy, sickle cell retinopathy, and other vascular disorders.
- Conducting basic research on retinal detachment to determine what stimulates and controls the abnormal cellular proliferation and membrane formation in the vitreous humor that increases the damage in this condition.
- Assessing the damaging effects of environmental factors, nutritional deficiencies, and drugs on retinal function, and developing screening systems for ocular toxicity.
- Pursuing new approaches to research on the basic biology, immunology, and genetics of sight- and life-threatening intraocular tumors.

# CORNEAL DISEASES

The cornea is the transparent tissue at the front of the eye which plays a key role in refracting or

bending light to focus images sharply on the retina. Because the cornea is the most exposed surface of the eye, it is particularly vulnerable to damage from injury, infection, toxic agents, and environmental pollutants.

Corneal diseases and injuries account for only about 6 percent of all legal blindness in the United States, but such disorders are the primary cause of blindness worldwide. In addition, they are the most painful of all ocular disorders and account for considerable disability. In the United States approximately 62 percent of all annual cases of eye diseases affect the cornea. They account for more than 100,000 hospital days, $12 million in surgical costs, and more than 8 million office visits annually for professional eye care. Eye injuries, which primarily affect the cornea, account for an additional 1.7 million annual visits to physicians.

Herpes simplex virus is the leading infectious cause of corneal blindness and visual impairment in the United States. Acute ocular herpes infections are difficult to treat, but a number of effective antiviral drugs are now available. In fact, most of the antiherpes drugs now on the market were first tested and proved effective in the eye, and research on ocular herpes and its treatment has made a major contribution to knowledge and treatment of herpes infections generally. Unfortunately, none of the present agents can prevent recurrences of ocular herpes due to reactivation of latent virus residing within nerve tissues behind the eye. Thus, further research on this painful and disabling condition is of high priority.

Changes in the ocular surface, frequently caused by aging, are another concern of the Corneal Diseases program. These changes can make the eye more vulnerable to injury and infection as the surface's protective effects are diminished. Research on contact lenses and surgical methods of refractive error correction is also a vital element of this program. Still another is corneal transplantation, one of the oldest and most successful of all tissue transplant procedures, which has restored sight to many thousands of people who would otherwise have been permanently blinded by corneal injury or disease. Research supported in the NEI Corneal Diseases program seeks to improve the success rate of corneal transplantation and extend its use to treating disorders which at present are not generally amenable to such therapy.

Other major targets of corneal disease research are corneal swelling resulting from disease or surgery, inherited and degenerative corneal diseases, and basic mechanisms involved in normal and abnormal corneal development and function.

The following are examples of the Council's recommended Program Development Priorities for the Corneal Diseases program:

- Determining the neuronal and viral factors contributing to the latent period of herpes infection.
- Continuing development of antiviral drugs for treatment of acute and recurrent corneal infections.
- Continuing development of methods to stimulate repair of the diseased or injured corneal endothelium (the tissue's innermost layer), especially in primates, and improving corneal transplant procedures using cultured endothelial cells as a possible replacement for donor tissue.
- Studying the biological effects of existing and proposed surgical procedures and optical devices for correcting refractive error.
- Evaluating immunological mechanisms of the ocular surface and their role in health and disease.
- Studying the frequently painful abnormalities of the ocular surface, their causes and persistence, and establishing their relationship to the cornea's nerve supply.
- Investigating the changes that occur with disease and aging in the biochemistry of the corneal stroma, the tissue's middle layer.
- Improving understanding of the biochemical and immunological components of the cornea's response to injury and wound healing, determining the importance of specific immunological factors in corneal transplantation, and developing and testing drugs that can modify or eliminate damaging immune reactions to transplanted tissue.

# CATARACT

A cataract is an opacity of the eye's normally clear lens that interferes with vision. Although usually occurring in old age, cataract may develop at any time in life, beginning even before birth. It may be a consequence of diabetes or other metabolic disorders, trauma, or exposure to toxic agents and radiation, or cataract may be inherited or congenital in nature.

About 60 percent of people between the ages of 65 and 74 show some signs of cataract, and about 3.3 million people in the United States are visually impaired by this disorder. At least 43,000 people are blind from cataract, making it the third leading cause of legal blindness in the United States; about 4,700 new cases of blindness from cataract occur each year.

At present, surgery to remove the opaque lens is the only effective way of treating cataract. Techniques developed over the past 25 years have made

cataract extraction one of the safest and most successful major operations. About 90 to 95 percent of the 475,000 cataract extractions performed each year in the United States at a total cost of $1.2 billion are successful in restoring useful vision when eyeglasses, contact lenses, or, in some patients, artificial lens implants are used. Nonetheless, because it is always desirable to avoid surgery if possible and because complications or unsatisfactory visual adjustments still occur following cataract extraction in a small percentage of cases, the National Eye Institute devotes most of its funding in the Cataract program to research aimed at developing means of preventing or slowing the development of cataract or of treating it nonsurgically. It has been estimated that if it were possible to slow the progression of cataract enough to delay the need for surgery by only ten years, the number of cataract operations performed in the United States could be reduced by 45 percent annually, resulting in a savings of over $530 million per year.

The following are examples of the Council's recommended Program Development Priorities for the Cataract program:

- Determining through epidemiologic studies factors that increase one's risk of developing cataract.
- Studying the molecular biology of the normal lens and cataract, with emphasis on gene analysis and the structure and metabolism of nucleic acids.
- Developing an objective system for classifying cataracts in the living eye as a standard for research on cataract prevention and treatment.
- Studying the biochemical and biophysical properties of lens crystallins, particularly with regard to transparency, and the structure and function of the cytoskeleton, those protein elements that help the lens maintain its shape.
- Studying the potentially cataract-inducing effects of low doses of ionizing and microwave radiation and the effects of environmental ultraviolet radiation on the lens.
- Comparing the results of various methods of cataract surgery and employing controlled clinical trials to determine the safety and efficacy of various methods of optical correction following cataract surgery, including intraocular lenses, contact lenses, and surgical modification of corneal curvature.
- Conducting further studies of the characteristics of the enzyme aldose reductase and developing safer and more effective aldose reductase inhibitors to delay diabetic cataract formation.

# GLAUCOMA

There are many types of glaucoma, most of which are characterized by an abnormally high level of the fluid pressure within the eye (intraocular pressure) accompanied by progressive destruction of peripheral vision due to irreversible damage to the optic nerve.

Although glaucoma may occur at any time in life, and there are severe congenital forms of the disease, the risk of developing glaucoma increases with age. Approximately 62,000 Americans are legally blind from glaucoma, and about 1.2 million Americans are known to have this disease. An equal number may be unaware that they have glaucoma. In addition, as many as 10 million people may have elevated intraocular pressure called "ocular hypertension," but show no optic nerve damage, although some will eventually develop glaucoma. Conversely, a significant number of people suffer optic nerve damage even though they have what is considered normal intraocular pressure. This condition is referred to as "low tension" glaucoma. At present, there is no sure way to predict which people, with or without ocular hypertension, are at risk for developing glaucoma or losing vision.

Normal intraocular pressure is maintained by balancing the continuous production of fluid within the eye and the rate of its drainage from the eye. This fluid, the aqueous humor, which is produced primarily by the ciliary body, passes between the iris and the lens and fills the *anterior chamber*, the space between the lens and cornea, thereby providing nourishment to these transparent tissues which have no blood supply. Fluid leaves the eye by filtering through the trabecular meshwork and the *canal of Schlemm*, the tissues located in the area enclosed by the *angle* formed by the juncture of the iris and the cornea. Almost always it is the blockage of the aqueous humor exit pathways, rather than overproduction of fluid, that is the cause for increased intraocular pressure in glaucoma.

Glaucoma is diagnosed by measuring intraocular pressure, observing typical changes in appearance of the *optic nerve head* with an ophthalmoscope, and measuring changes in the field of vision. Because the progress of glaucoma often can be stopped or at least slowed by drugs or surgery to reduce intraocular pressure, blindness can usually be prevented if the condition is detected and treated early. However, once vision is damaged or lost because of glaucoma, it cannot be restored.

Although glaucoma may be controlled, most forms of the disease cannot be cured. The predominant form of glaucoma, accounting for up to 80 percent of all cases of the disease, is known as primary open-angle glaucoma. In this condition and in

ocular hypertension and low tension glaucoma, outflow of aqueous humor is impaired although no anatomic blockage is apparent in the filtration angle. Current research is focused on possible mechanisms involving submicroscopic particles which may clog the filtration channels.

Angle-closure glaucoma, which accounts for 10 to 20 percent of all glaucoma cases, is characterized by a narrower than normal filtration angle, caused by the iris and lens being closer to the front of the eye than they are in unaffected people. Intraocular pressure rises when aqueous humor outflow is impeded by the iris being pushed closer to the cornea, thus closing off the angle. In some patients this condition can be controlled by drugs. In other cases, cutting a tiny hole in the iris can cure the disorder.

The fact that glaucoma remains a major cause of blindness, despite the availability of various ways of controlling intraocular pressure, indicates the need to understand better the mechanisms by which increased intraocular pressure causes optic nerve damage and to develop more effective means of early detection, prevention, and treatment.

Treatment for glaucoma, whether by drugs or surgery, is aimed either at diminishing aqueous humor production or at facilitating its outflow. In the search for a cure for glaucoma, an understanding of the normal cellular processes that regulate the flow of aqueous humor through the eye, how they are changed as the disease is initiated and progresses, and how drugs act upon them is essential, as is determining how optic nerve damage is related to intraocular pressure. An understanding of the basic physiologic processes in the optic nerve which are affected in glaucoma should ultimately lead to the development of ways to protect the optic nerve and perhaps eventually to reverse nerve damage.

The following are examples of the Council's recommended Program Development Priorities for the Glaucoma program:

- Conducting clinical and laboratory studies to define genetic, racial, and environmental risk factors for the development of damage to the optic nerve in glaucoma and to determine the reasons for the varying susceptibilities of individual eyes to optic nerve damage.
- Developing improved methods of detection and diagnosis and better drug and surgical treatments for glaucoma.
- Devising new noninvasive clinical techniques for studying aqueous humor formation and flow, for continuous monitoring of intraocular pressure in man and in primates, and for studying experimental optic nerve damage in monkeys.
- Studying the cell biology and molecular characteristics of the outflow tissues and their abnormalities in glaucoma, especially using tissue and organ culture techniques.
- Exploiting experimental methods of studying the basic physiology and pharmacology of fluid movement in the eye and of controlling aqueous humor inflow in primates and in man.
- Investigating neovascular glaucoma which results from the formation of abnormal blood vessels on the iris that overgrow the angle, often occurring as a severe complication of certain retinal vascular diseases, and developing methods for its treatment.
- Establishing eye donor programs so that appropriately obtained and preserved human tissues from well-characterized glaucoma patients will become available for correlations between clinical history and tissue damage and for cell biology studies.

## STRABISMUS, AMBLYOPIA, AND VISUAL PROCESSING

Seeing involves a series of highly complex events that begin the instant light enters the eye and images fall onto the retina and continue until objects are perceived in all their detail, depth, and color. The act of seeing is always accompanied either by purposeful targeted eye movements or by searching and scanning movements. It is further refined by turning the eyes inward (convergence) when looking at nearby objects or outward (divergence) when looking at objects farther away. A disturbance of any one of the many parts of the elaborate and precisely controlled systems for ocular development, information processing, or eye movements can lead to serious visual impairment such as amblyopia (severely reduced vision in one eye—often called "lazy eye"), strabismus (misalignment of the eyes—cross-eye or walleye), nystagmus (irregular eye movements), myopia (nearsightedness), defects in the field of vision, or other conditions that require very strong corrective lenses. These conditions collectively affect over 10 percent of the population. Although they seldom cause legal blindness, they produce considerable visual impairment and disability, interfere with learning and working, and even cause psychological problems because of their effect on appearance.

The NEI Strabismus, Amblyopia, and Visual Processing program supports research on the structure, function, development, and disorders of those

portions of the brain and extraocular muscle system that serve vision. These studies are directed toward gaining a better understanding of normal vision as well as determining the causes of visual deficits and blindness that do not appear to be due to specific dysfunction of the eye itself. Understanding visual processing and the disorders that affect it is almost totally intertwined with knowledge of how the human nervous system works. This includes molecular, cellular, genetic, and chemical aspects, how nerve impulses are transmitted and integrated, and the resultant perceptual and motor responses. The continued advancement of clinical investigation of normal and abnormal visual processing depends upon an improved understanding of basic visual mechanisms. Only by supporting both basic and clinical research can new methods be developed for preventing, diagnosing, and treating visual sensory and motor disorders.

The following are examples of the Council's recommended Program Development Priorities for the Strabismus, Amblyopia, and Visual Processing program:

- Developing new or improved techniques for treating strabismus, including surgical, pharmacological, or other approaches; evaluating the most promising techniques in controlled trials; and determining how the timing of treatment influences success.
- Developing and evaluating new treatments for amblyopia, including eye patching, contact lenses, or pharmacological approaches.
- Devising noninvasive methods for studying the development of visual processing in infants, particularly methods that could be used in the clinic for diagnosing and monitoring the effects of treatment.
- Studying the normal development and control of the eye movement system and the disorders that may affect it, especially using techniques that will aid in diagnosing eye muscle problems in newborns and young children.
- Determining the causes of and mechanisms responsible for the development of myopia in humans, expanding studies with animal models, and relating the results of animal studies to the human condition.
- Investigating the structure, function, and development of the visual system at the molecular level—including studies of cellular receptor sites, cell specificity, neurotransmitters and peptides, and immunological approaches—with the ultimate aim of designing drug treatments for visual neurosensory disorders and injuries.
- Studying the anatomy, physiology, and behavior of the systems that are important in vergence (moving the two eyes toward or away from each other to look at a nearby or distant object) and accommodation (changing the shape of the lens to allow the eye to focus on an object) in normally developing infants as well as in those at risk for strabismus.
- Exploring the etiology of optic neuritis and optic nerve atrophy and those factors that may permit regeneration of the diseased or injured optic nerve.

# VISUAL IMPAIRMENT AND ITS REHABILITATION

A wide diversity of visual characteristics and rehabilitative needs exists among visually impaired persons. Unfortunately, studies of visual impairment and rehabilitation of the affected population have not flourished as has biomedical research in general. As a result, the needs of visually impaired people have not been addressed in a comprehensive fashion.

The visually impaired population includes not only blind people, but also those who are partially-sighted. Losses in visual acuity experienced by these people may range from slight to profound; visual field loss may be predominantly peripheral or predominantly central; other visual functions such as dark adaptation, color vision, and contrast sensitivity may be impaired; or there may be increased sensitivity to glare. Handicaps resulting from impaired vision include diminished ability to read, to recognize faces and facial expressions, to perform visually guided motor tasks, to be aware of the important features of one's immediate environment, or to see at night. The extent of the disability created by the visual impairment depends not only on the nature and extent of the visual loss, but also on the needs, aspirations, attitudes, and physical abilities of the individual.

Although research on the prevention, diagnosis, and treatment of eye diseases and vision disorders offers the best hope for reducing blindness, also needed are studies aimed at helping those who already have irreversibly impaired vision. To meet this need, the National Eye Institute supports research aimed at enabling partially sighted and totally blind people to perform important tasks in school, at the workplace, or in leisure activities. Part of this research is directed at better characterization of the effect of specific diseases on vision, one goal of which is to help people with such

problems make the most effective use of their remaining sight. Research is also needed in the design, development, and evaluation of optical aids, video-magnification or image enhancement systems, methods for training people with impaired central vision to use their peripheral vision more effectively, and other techniques aimed at improving performance of visual tasks and substituting partially or completely for lost vision.

There is a major need to develop, organize, and coordinate research on Visual Impairment and Its Rehabilitation, whether supported by NEI or other government or private organizations. Initial steps toward this organization and improved communication are now being taken. Also needed are broadly based programs that offer different research approaches, as well as wide-ranging clinical and basic research training programs.

The following are examples of the Council's recommended Program Development Priorities for the Visual Impairment and Its Rehabilitation program:

- Defining the visual characteristics of individuals with specific types of visual impairments.
- Conducting research on the optical, electronic, and other rehabilitative needs of visually impaired persons.
- Conducting research on improving basic skills relating to mobility and visual orientation in the low vision population.
- Encouraging human engineering studies that will help people with specific impairments interact more independently with their environment.
- Conducting epidemiological studies of the types and extent of visual impairment resulting from a variety of disorders.
- Developing aids, including contact lenses and other specialized lenses, for patients with corneal or lens problems.
- Studying the effects of prior visual experience upon the nature and extent of visual impairment in young children and on their ability to function despite such impairment.

# RESOURCE REQUIREMENTS

After making a grant-by-grant analysis and assessment of current support in each NEI program, as well as of vision-related research projects supported by other Federal and private organizations, the Council and its planning panels developed estimates of the numbers of projects that would be required to implement the Program Base and Program Development Priority recommendations in each NEI program in FY 1983 (Table). The dollar value of these projects was then calculated by using estimates of the average cost of a grant for FY 1983 in each program. Cost estimates for FY 1984 and FY 1985 represent approximately a 9 percent increase over the preceding year, including 5 percent for inflation. Because of increasing uncertainties in the annual Federal budget, the Council did not recommend a budget for the final two years covered by the plan, but intends to revise and extend its estimates periodically.

In making these recommendations, the Council and its consultant panels took the following factors into consideration in each area of research:

- Degree of relevance to NEI program goals and objectives
- Current level of support
- Recent research accomplishments
- Potential for future development
- Availability of trained manpower
- Likelihood of significant progress over the next three to five years

In the Table, the amounts in parentheses represent the total number and dollar value, actual (FY 1981) or estimated (FY 1982-1985), of NEI research awards—individual Research Project Grants, Small Grants for Pilot Projects, New Investigator Research Awards, Research Career Awards, and Specialized Clinical Research Centers—included within each program. The total shown for each program includes, in addition to these mechanisms, National Research Service (training) Awards, Core Grants, Research Contracts, Scientific Conference Grants, and other types of research support. (Each of these mechanisms is defined in *Volume Three, Support for Vision Research*. In *Volume One*, Chapter Three, "Summary Panel Reports and Resource Requirements," more detailed tables show the allocation of current and recommended projects and dollars to each of the several subprograms within the five programs. Included in *Volume Two* are tables that further categorize these recommendations within the Program Base and Program Development Priorities for each subprogram.)

The Council's purpose in developing these recommendations is to provide a rational estimate of the resources needed to carry out this research plan at a reasonable level of activity during the fiscal years 1983-1985 and to set priorities for the expenditure of whatever funds the Congress and the President ultimately make available to the NEI for these years.

## National Advisory Eye Council Planning Budget for the National Eye Institute by Activity FY 1983–1985

**(Amounts in Thousands)[1]**

| | 1981 Actual | | 1982 Estimate | | 1983 NAEC Estimate | | 1984 NAEC Estimate | | 1985 NAEC Estimate | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. | Amount | No. | Amount | No. | Amount | No. | Amount | No. | Amount |
| **Extramural Research** | | | | | | | | | | |
| Retinal and Choroidal Diseases | | $ 42,322 | | $ 46,078 | | $ 62,552 | | $ 68,502 | | $ 74,482 |
| | (381) | (33,577) | (395) | (36,085) | (492) | (51,660) | (515) | (56,574) | (535) | (61,513) |
| Corneal Diseases | | 16,769 | | 17,803 | | 25,085 | | 27,472 | | 29,869 |
| | (162) | (15,849) | (167) | (17,020) | (215) | (23,005) | (225) | (25,194) | (230) | (27,392) |
| Cataract | | 9,723 | | 10,651 | | 16,356 | | 17,912 | | 19,475 |
| | (101) | (8,970) | (106) | (10,092) | (137) | (14,796) | (140) | (16,204) | (150) | (17,618) |
| Glaucoma | | 9,950 | | 10,865 | | 16,540 | | 18,114 | | 19,694 |
| | (90) | (8,780) | (98) | (9,843) | (125) | (14,500) | (130) | (15,880) | (135) | (17,265) |
| Strabismus, Amblyopia, and Visual Processing | | 23,125 | | 22,527 | | 36,744 | | 40,240 | | 43,752 |
| | (268) | (22,070) | (258) | (21,620) | (353) | (34,594) | (370) | (37,885) | (380) | (41,192) |
| Visual Impairment and Its Rehabilitation | | 166[2] | | 513[2] | | 2,794 | | 3,060 | | 3,328 |
| | (4) | (166) | (5) | (513) | (27) | (2,794) | (30) | (3,060) | (30) | (3,328) |
| **Subtotal, Extramural Research** | | **$101,889** | | **$107,924** | | **$160,071** | | **$175,300** | | **$190,600** |
| | **(1,006)** | **(89,412)** | **(1,029)** | **(95,173)** | **(1,349)** | **(141,349)** | **(1,410)** | **(154,797)** | **(1,460)** | **(168,308)** |
| **Intramural Research** | | | | | | | | | | |
| NEI Laboratory and Clinical Research | | 6,346 | | 6,544 | | 8,275 | | 8,900 | | 9,600 |
| Office of Biometry and Epidemiology | | 686 | | 750 | | 825 | | 900 | | 1,000 |
| NIH Management Fund[3] | | 4,543 | | 5,111 | | 5,900 | | 6,400 | | 6,900 |
| **Subtotal, Intramural Research** | | **11,575** | | **12,405** | | **15,000** | | **16,200** | | **17,500** |
| **Direct Operations** | | | | | | | | | | |
| NEI Extramural Management | | 1,657 | | 2,144 | | 2,587 | | 2,800 | | 3,000 |
| NEI Program Management[4] | | 1,345 | | 1,533 | | 1,800 | | 1,900 | | 2,000 |
| NIH Management Fund[5] | | 1,260 | | 1,368 | | 1,713 | | 1,800 | | 1,900 |
| **Subtotal, Direct Operations** | | **4,262** | | **5,045** | | **6,100** | | **6,500** | | **6,900** |
| **Construction** | | — | | 2,000 | | 10,000 | | 10,000 | | 10,000 |
| **Total, NEI** | | **$117,726** | | **$127,374** | | **$191,171** | | **$208,000** | | **$225,000** |

[1] Numbers in parentheses indicate the total number and amount for individual Research Project Grants, Small Grants for Pilot Projects, New Investigator Research Awards, Research Career Awards, and Specialized Clinical Research Centers included within each program estimate.

[2] No specific appropriation is currently authorized for Visual Impairment and Its Rehabilitation. Grants funded in this area are paid from whichever of the preceding five programs seems most appropriate to the purpose of a given study, usually either the Retinal and Choroidal Diseases program or the Strabismus, Amblyopia, and Visual Processing program.

[3] This portion of the Management Fund is an assessment for NIH central services that support research conducted at the NIH campus in Bethesda, Maryland. These services include operation of the NIH Clinical Center, engineering services, utilities, computer services, and other research services.

[4] Supports the NEI Office of Director and overall NEI management.

[5] This portion of the Management Fund is an assessment for NIH central services that support the general management and program direction of the NEI. These services include central NIH receipt and review of research grant applications, centralized NIH financial management, and other administrative services.

The foregoing is a brief condensation of *Vision Research—A National Plan: 1983-1987*, abstracting its major sections. Other sections of the plan should be consulted for a fuller understanding of the issues raised and conclusions drawn in this Executive Summary.

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